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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,136	04/16/2004	Nobert Hofgen	HUBR-1261-US	8765
24972	7590	09/06/2006		
FULBRIGHT & JAWORSKI, LLP 666 FIFTH AVE NEW YORK, NY 10103-3198				
			EXAMINER BALLS, ROBERT J	
			ART UNIT 1625	PAPER NUMBER

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/826,136

Applicant(s)

HOFGEN ET AL.

Examiner

R. James Balls

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 June 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4-9,18-20 and 27-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-9,18-20 and 27-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

1. Claims 1-2, 4-9, 18-20 and 27-29 are pending.
2. This application claims benefit of foreign application, Gerday 103 18 610.7 filed April 24, 2003.
3. Claims 1-2, 4-9, 18-20 and new claims 27-29 are currently under examination.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 27-29 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims contain minor grammatical errors.
  - A. Claim 27 states that the "heteroatom is (i) are N, O or S." The word, "is" is probably meant to be "in."
  - B. Claims 27-29 use the term "heteroatom" in the singular but provide a plurality of options, i.e. N, O or S. Making the word, "heteroatom" plural would be clearer so that the claim reads, "...wherein the [heteroatom] heteroatoms [is] in (i) are N, O or S."

***Double Patenting***

5. The provisional rejection of Claims 1-2, 4-9, 18-20 (and new Claims 27-29 as necessitated by applicants' amendment) on the ground of nonstatutory obviousness-type double patenting over Claims 1-3, 5 and 9-18 of copending application no. 10/399,051 in view of Hatzelmann & Schudt, *Anti-inflammatory and Immunomodulatory Potential of the Novel PDE4 Inhibitor Roflumilast in Vitro*, J. PHARMACOL. & EXP. THER., 297:267-279 (2001) is maintained for the reasons of record.

Applicants contend that the instant rejection is improper pointing out that that the chemical structure of roflumilast (and its corresponding N-oxide) differs from the instant compounds and argue that any extrapolation therefrom is improper. Indeed, the overall chemical structure of roflumilast differs from the instant compounds. The instant rejection however, is not based on structural similarity of the co-pending claimed compounds but on the drug/metabolite correlation.

Compound claims are inherently anticipated by a prior art disclosure of a pharmaceutical drug that metabolizes into the claimed compound. See *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373 (Fed. Cir. 2003). The court explains that granting patent protection to a metabolite would allow the patentee to improperly extend patent protection by excluding the public from practicing the prior art (i.e. a patent broadly drawn to the parent drug is prima facie obvious over the metabolite). *Id.* at 1379.

The state of the art suggests that the N-oxide compounds of the instant claims are metabolites of the compounds claimed in the copending application. See Milano,

*Active Drug Metabolites*, CLINICAL PHARMACOKINETICS 10:216-227 (1985). Milano explains that nearly all drugs transform into metabolites *in vivo* and outlines the metabolic life cycle of different drugs. Specifically, Hatzelmann & Schudt show that roflumilast, also a PDE4 inhibitor with a pyridyl ring metabolizes into a N-oxide pyridyl *in vivo*. The N-oxide pyridyl metabolite is more potent than its parent drug. See page 277, first paragraph of the Discussion section. Applicants have also cited art showing that N-oxide pyridine derivatives of corresponding pyridine compounds exhibit PDE4 inhibitory activity, albeit less than the parent compounds. See applicants' response to the previous Detailed Action on the bottom of page 9 citing Hulme et al., *Optimum Anilinopyrimidien Substituents for CRH1-R Potency*, J. MED. CHEM., 8:3053-3058 (1998). This technical report provides the level of skill in the active metabolite art and supports the court decision of *Schering*. Therefore, absent factual evidence of unexpected results, the co-pending broad claims inherently encompass the narrower metabolic claims of the instant application.

The copending application broadly encompasses what is narrowly claimed in the instant application except that the instant application requires N-oxide pyridyl instead of free pyridyl. The claims of copending application no. 10/399,051 provide that R<sup>2</sup> may be pyridyl among other Markush alternatives. The instant claims are limited to compounds where R<sup>2</sup> is N-oxide pyridyl. Thus, an obvious-type double patenting rejection has been applied instead of an anticipatory rejection under 35 USC §102.

***Conclusion***

6. No Claims are allowed.
7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to R. James Balls whose telephone number is (571) 272-7997. The examiner can normally be reached on Mon - Fri 8:00am - 4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tom McKenzie can be reached on (571) 272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

R. James Balls  
28 August, 2006



Celia Chang  
Primary Examiner  
Art Unit 1625